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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,508	11/07/2001	Beerelli Seshi	0152.00418	8090

7590

04/25/2003

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EXAMINER

AFREMOVA, VERA

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 04/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
**09/914,508**

Applicant(s)  
**Seshi et al.**

Examiner  
**Vera Afremova**

Art Unit  
**1651**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on Jan 30, 2003
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 21-41 is/are pending in the application.
- 4a) Of the above, claim(s) 21 and 26-41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 22-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some\* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_  
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

Applicant's election with traverse of the group I invention, claims 22-25, in Paper No. 7 filed 1/30/2003 is acknowledged. The traversal is on the ground(s) that all groups of the claims relate to pluri-differentiated cells and should be examined together in order to promote efficiency of prosecution. This is not found persuasive because the claimed inventions lack unity as explained in the prior office action. The requirement is still deemed proper and is therefore made FINAL.

Claims 21 and 26-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claims. Applicant timely traversed the restriction requirement in Paper No. 7.

Claims 22-25 are under examination in the instant office action.

#### ***Claim Rejections - 35 USC § 112***

Claims 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-25 are indefinite with regard to characterization of the claimed cells. The as-filed specification does not provide definitions for the term "progenitor". Thus, this term is given broad interpretation drawn to a cell which is not terminally differentiated, which is capable to differentiate or which is pluri-potential, for example: a stem cell. According applicants' definitions the term "pluri-differentiated" refers to a single type cell co-expressing genes specific for multiple

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lineages (specification page 12, par. 2). However, it is uncertain what are the multiple lineages which are intended for the claimed cells. It is uncertain when and/or under what conditions gene expressions of multiple lineages occur. For example: does it occur simultaneously at identical conditions in the same culture system? Furthermore, the claimed invention refers to "cells". Thus, it is uncertain whether cells of a single type cell or of one clone are claimed. It is uncertain whether a mixed population of mesenchymal progenitor cells is claimed wherein the mixed population comprises cells expressing genes specific for cells of multiple or various lineages. Therefore, the term "pluri-differentiated" is given broad interpretation based on applicant's definitions as disclosed in the as-filed specification drawn to "co-expressing genes specific for multiple lineages" under the same conditions or under conditions specific for the expression of specific lineage.

Claim 25 is rendered indefinite by the abbreviated phrase "GvHD". Abbreviation in the first instance of claims should be explained upon with the abbreviation indicated in parentheses. The abbreviations can be used thereafter.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Pittenger et al. [U] in the light of teaching by Ager et al. [X].

Claim is directed to isolated mesenchymal progenitor cells that are pluri-differentiated.

Pittenger et al. [U] discloses isolated mesenchymal stem cells which are capable to differentiate towards cells of mesenchymal tissues (abstract) and thus, they are mesenchymal “progenitor” cells within the meaning of the claims. The mesenchymal stem cells of the cited reference are “pluri-differentiated” cells because they are capable to differentiate towards cells of multiple lineages including adipocytic, chondrocytic or osteocytic under particular conditions for particular lineages (figure 2). With respect to the applicant’s definitions, the mesenchymal stem cells of the cited reference are also “pluri-differentiated” because they are single type cells which simultaneously and at the same conditions co-express genes of cells of multiple lineages including surface proteins identified with various markers, for example: CD29, CD44, CD71, etc. (see page 144, col. 1) which are also expressed by fibroblasts, keratinocytes, epithelial cells, endothelial cells, muscle cells, myocytes in the light of teaching by Ager et al. [X]. Thus, the mesenchymal stem cells of the cited reference are considered to anticipate the claimed invention within the meaning of the claims and in the light of as-filed specification.

Claims 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by US 6,010,696 [A].

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Claims are directed to isolated mesenchymal progenitor cells that are pluri-differentiated and to therapeutic compositions comprising isolated pluri-differentiated mesenchymal progenitor cells in amounts effective for treating a disease state in a mammal or to enhance hematopoietic progenitor cell engraftment in a mammal.

The cited patent US 6,010,696 discloses isolated mesenchymal progenitor cells that are pluri-differentiated such as mesenchymal stem cells capable to differentiate into cells of various types of skeletal and connective tissues depending upon environmental influences (col. 1, lines 25-42). The cited patent also discloses therapeutic compositions comprising these cells in amounts effective for treating a disease state in a cancer mammal patient (example 3) or to enhance hematopoietic progenitor cell engraftment in a mammal patient (col. 3, lines 13-30).

The mesenchymal stem cells of the cited patent are considered to be identical to the presently claimed cells because they are non-terminally differentiated cells and, thus, they are "progenitor" cells as claimed and because they are taught as being capable to differentiate towards cells of various lineages and, therefore, they are "co-expressing genes specific for multiple lineages" as the presently claimed "pluri-differentiated" mesenchymal progenitor cells according applicant's definitions (see disclosure at page 12, paragraph 2). Furthermore, the cited mesenchymal stem cells are considered to be identical to the presently claimed cells particularly in view that the cited cells are taught to be effective for identical purpose of treating disease state in mammals who are in need of engraftment of hematopoietic progenitor cells as required by the presently claimed invention.

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***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,010,696 [A] and Pittenger et al. [U] in the light of Ager et al. [X] and Bordignon et al. [V].

Claims are directed to isolated mesenchymal progenitor cells that are pluri-differentiated and to therapeutic compositions comprising isolated pluri-differentiated mesenchymal progenitor cells in amounts effective for treating a disease state in a mammal, for enhancing hematopoietic progenitor cell engraftment in a mammal and/or for treating graft-versus-host-disease (GvHD) in mammal about to undergo bone marrow or organ transplantation.

Both cited references US 6,010,696 [A] and Pittenger et al. [U] teach isolated "mesenchymal progenitor cells that are pluri-differentiated" as explained above and compositions with these cells.

US 6,010,696 [A] also teaches therapeutic compositions comprising mesenchymal pluri-differentiated progenitor cells or mesenchymal stem cells in amounts effective for treating a disease state in mammals and/or to enhance hematopoietic progenitor cell engraftment in

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mammals. Although the reference by Pittenger et al. [U] is lacking particular disclosure related to therapeutically effective amounts of mesenchymal pluri-differentiated progenitor cells or mesenchymal stem cells in cellular compositions, it suggests application of these cellular compositions for restoration of damaged or diseased tissues (page 146, col. 2, last lines of the paragraph 2).

The cited references US 6,010,696 [A] and Pittenger et al. [U] are lacking particular disclosure related to treating graft-versus-host-disease (GvHD) in mammal about to undergo bone marrow or organ transplantation with compositions comprising mesenchymal pluri-differentiated progenitor cells or mesenchymal stem cells. But the reference by Bordinon et al. [V] teaches and/or suggests clinical applications of mesenchymal stem cells for treating various disease state in mammals including modulation of graft-versus-host-disease (GvHD), autologous and allogeneic replacement of damaged tissues and enhancement of hematopoietic progenitor cell engraftment or transplantation (table 4, page 1138).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to obtain therapeutic compositions comprising effective amounts of mesenchymal progenitor pluri-differentiated cells or mesenchymal stem cells with a reasonable expectation of success in treating various disease states in mammals including treating GvHD and/or enhancing hematopoietic progenitor cell engraftment or tissue transplantation because mesenchymal stem cells have been known and taught in the prior art as clinically suitable and therapeutically effective for treating various disease state in mammals including treating GvHD



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and/or enhancing hematopoietic progenitor cell engraftment or tissue transplantation. It is considered to be within the purview of one of ordinary skill in the art to adjust effective amounts of cells in the therapeutic cellular compositions depending on a particular protocol of clinical treatment and/or severity of disease state or patient condition. Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

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April 11, 2003

VERA AFREMOVA

PATENT EXAMINER

